UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,302	01/17/2002	Kyung Jin Kim	A-67640-2/RFT/NBC	6859

23552 7590 04/10/2007

MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/053,302	KIM ET AL.	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-11,14,15,17,19,21 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-11,14,15,17,19,21 and 23-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-18-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment to the specification and claims filed January 18, 2007 is acknowledged.

   Claims 2, 4, 12, 13, 16, 18, 20 and 22 have been canceled.

   Claims 7-11, 14, 15, 19 and 23 have been amended.

   Claims 24-29 are new.

   Claims 1, 3, 5-11, 14, 15, 17, 19, 21 and 23-29 are pending.

   Claims 1, 3, 5-11, 14, 15, 17, 19, 21 and 23-29 are under examination as they read on anti-IFNAR2 antibodies.

2. The rejections of record can be found in the previous Office Action, mailed August 18, 2006.

   This Office Action is in response to Applicant's response filed January 18, 2007.

   The previous objections to the specification and claims have been withdrawn in view of applicant's amendments.

   The previous rejection under 35 U.S.C. § 112, 2nd paragraph has been withdrawn in view of applicant's argument.

   The previous rejection under 35 U.S.C. § 112, 1st paragraph, enablement with respect to a deposit of the claimed hybridomas has been withdraw in view of applicant's amendment to the specification and assurances regarding the public availability submitted on June 24, 2004.

   New Grounds of Rejection are set forth below.

3. Applicant's request for an interview on page 14, last paragraph of applicant's remarks is acknowledged. However, due to administrative deadlines this Office Action is being set forth. Moreover, New Grounds of Rejection necessitated by applicant's amendment to the claims are set forth below. Should applicant wish to discuss any matter related to applicant's effort to draft a response to the instant Office Action or any outstanding Office Action in the future, applicant is encouraged to call the examiner to schedule an interview before any action from the Office to applicant comes due.

4. Claims 10, 11 and 14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

This is a New Grounds of Rejection necessitated by applicant's amendment to the claims.

Claims 10 and 11, and dependent claims thereof, recite the antibody of claim 8 wherein said antibody is a humanized or human antibody, respectively.

However "the antibody of claim 8" is limited to a very specific antibody: the 1D3 murine antibody produced by the hybridoma cell line with ATCC Accession No. HB12428. Thus, claims 10 and 11, and dependent claims thereof, fail to further limit claim 8 because a murine antibody with a particular amino acid sequence cannot be further limited to be a humanized antibody or human antibody.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 24-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a New Matter rejection/New Grounds of Rejection necessitated by Applicant's amendment to the claims filed October 25, 2006.

In particular, claims 24-26 recite, "an anti-IFNAR2 antibody that ***blocks the antiviral activity*** of a first type I interferon...binds to IFNAR2 and does not bind to IFNAR2 comprising an alanine at one or more amino acids...."

Applicant points to page 30, lines 14-24, page 32, lines 4-17 and page 34, lines 4-26 in support of these claims.

The specification as filed does not provide sufficient blazemarks or direction for the instant claims. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

In particular, applicant is claiming a subgenus not sufficiently supported by the specification as-filed. For example, in support of the instant claims applicant points to the disclosure on page 34, lines 4-26 which states:

"For example, the invention provides anti-IFNAR2 antibodies and Fv clones which bind to one or more of amino acid positions 133, 134, 135, and 139 in situ in the sequence of IFNAR2, which bind to one or more of amino acids 153, 154 and 156 in situ in the sequence of IFNAR2, which ***block the binding*** of a first type I interferon to IFNAR2, and which ***do not block the binding*** of a second type I interferon to IFNAR2. Such Fv clones can be selected by (1) isolating anti-IFNAR2 clones from a phage library as described in Section B(I)(2) above, and optionally amplifying the isolated population of phage clones by growing up the population in a suitable bacterial host; (2) selecting a first type I interferon and a second type I interferon against which blocking and non-blocking activity, respectively, is desired; (3) adsorbing the anti-IFNAR2 phage clones to immobilized IFNAR2;.....(7) eluting the clones which remain adsorbed following step (6); (8) adsorbing the eluted clones to an immobilized, mutant IFNAR2 containing an Ala substitution at amino acid positions 133, 134, 135, and 139 in the sequence of IFNAR2 in order to adsorb undesired clones which bind to determinants on IFNAR2 that do not overlap with the amino acid positions 133, 134, 135, or 139; (9) recovering the clones which fail to adsorb to immobilized, mutant IFNAR2 from the flow-through fractions in step (8); and (10) repeating steps (8) and (9) in order to screen the recovered clones for non-adsorption to the corresponding immobilized, Ala-substituted mutant IFNAR2 for amino acid positions 153, 154 and 156."

This disclosure appears to be most related to claim 24.

However, while the instant specification provides literal written support for anti-IFNAR2 antibodies that ***"block the binding"*** of a first Type I interferon to IFNAR2 and do not block the binding of a second type I interferon to IFNAR2 and which does not bind to IFNAR2 comprising an alanine at one or more amino acids 133, 134, 135, 139, 153, 154, and 156, the instant specification ***does not support*** the particular subgenus of anti-IFNAR2 antibodies that ***"block the antiviral activity"*** of a first type interferon...

A generic or a sub-generic disclosure cannot support a species unless the species is specifically described.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Furthermore, while the instant specification discloses the following at page 42, 3rd paragraph: "[i]n another example, the invention provides an anti-IFNAR2 antibody that binds to one or more of amino acid positions 133, 134, 135, and 139 in situ in the sequence of IFNAR2, binds to one or more of amino acids 153, 154 and 156 in situ in the sequence of IFNAR2, inhibits the anti-viral activity of a first type I interferon, and does not inhibit the anti-viral activity of IFNβ," this is ***not*** the same as what is now instantly claimed.

In particular, ***in contrast to the disclosure at page 42, 3rd paragraph***, the instant claims recite **(a) generic "blocking of the anti-viral activity"** of a first type I interferon, a term which does not appear to be defined in the instant specification (whereas the term "inhibiting of the anti-viral activity" is defined, for example at page 39, 1st paragraph) and **(b)** that the antibody "does ***not*** bind IFNAR2 comprising an ***alanine*** at one or more amino acids...," a negative limitation which the passage at page 42 does not support in that it does not *necessarily direct* the skilled artisan to make anti-IFNAR2 antibodies that block anti-viral activity and do not bind IFNAR2 comprising an ***alanine*** at one or more amino acids 133, 134, 135, 139, 153, 154 and 156.

Thus, the instant claims recite limitations which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action.

Alternatively, applicant may provide sufficient written support for the limitations indicated above. See MPEP 714.02 and 2163.06

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **Claims 5-11, 14, 21 and 24-26 are rejected under 35 U.S.C. § 112, first paragraph,** as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A. Blocking vs. Non-blocking monoclonal antibodies: Claims 5-11, 14 and 21

Applicant argues that they "have exemplified at least one antibody that substantially block activity or binding of a Type I interferon to IFNAR2 and does not block the antiviral activity of a second type I interferon...1D3..." (see applicant's remarks, page 10, emphasis in the original).

Applicant's arguments have been considered but have not been found convincing, essentially for the reasons of record.

Applicant's remarks that they "have exemplified ***at least one*** antibody that substantially block activity or binding of ***a*** Type I interferon to IFNAR2 and does not block the antiviral activity of a second type I interferon...***1D3***..." seems to be imply that applicant believes the limitations of the instant claims are applicable ***only*** to the 1D3 antibody and not the other antibodies recited in base claim 1.

However, as put forth in the previous Office Action, the instant claims, given their broadest reasonable interpretation consistent with the instant specification, read on ***each*** of the antibodies recited in base claim 1, wherein said antibodies are further limited by the recitations of the claims which depend from claim 1.

Thus, ***with respect to the 1F3 and 3B7 antibodies***, these antibodies do not meet the limitations of the instant claims because they block the biological activity of ***all*** interferons tested in the instant specification, including ***IFNα-2/1 and IFNβ***. Accordingly, the instant specification does **not** provide sufficient direction or guidance to enable one of skill in the art ***to make*** monoclonal antibodies 3B7 and 1F3 with the properties recited in the instant claims because these monoclonal antibodies ***block the binding, anti-viral activity and IGSF complex formation for all the interferons tested*** according to the instant specification. Moreover, these antibodies ***do not compete with the 1D3*** for binding to IFNAR2 in a competitive ELISA according to the instant specification at page 68, 2nd paragraph through page 69, 1st paragraph.

Thus, undue experimentation would be required to produce the claimed invention commensurate with the scope of the claims from the written disclosure alone. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

B. Antibodies that do not bind IFNAR2 with one or more alanine substitutions: Claims 24-26

Claims 24-26, recite an anti-IFNAR2 antibody which "***does not bind to IFNAR2*** comprising an alanine substitution at one or more amino acids..."

Claims to an anti-IFNAR2 antibody that "***does not bind to IFNAR2",*** given their broadest reasonable interpretation consistent with the instant specification, read on anti-IFNAR2 antibody that ***binds an IFNAR2 alanine mutant with less than at or about 90% of the activity with which it binds wild type hIFNAR2***. See instant specification at page 29, 1st paragraph.

However, the instant specification does not provide sufficient guidance or direction to make antibodies encompassed by the breadth of the instant claims.

In particular, while the instant specification discloses, for example, an antibody that blocks the binding of a first type I interferon to IFNAR2, but does not block the binding of a second type I interferon to IFNAR2, such as IFNβ, and which exhibits binding activity with IFNAR2 comprising an alanine at amino acids 133, 134, 135 and 139 which is less than at or about 10% of the binding that this particular antibody would have for wt IFNAR2 (see instant specification at page 72, table 3, row 7, and the 1D3 antibody), the instant specification does disclose how to make ***all*** of the antibodies encompassed by the instant claims that ***bind an IFNAR2 containing one or more alanine substitutions with less than at or about 90% of the activity with which the antibody binds wild type hIFNAR2***.

For example, the only antibody disclosed in the instant specification that may meet the limitations of claim 24 regarding anti-viral activity, the 1D3 antibody ***binds*** to IFNAR2 with a substitution at K153A (see, instant specification, for example page 73, Table 4).

Moreover, the antibodies exemplified in the instant specification that meet the antiviral limitation of claims 25 and 26, such as the 1D3, 1F3 and 3B7 monoclonal antibodies as well as the disclosed polyclonal anti-IFNAR2 antisera, all ***bind*** to IFNAR2 with substitutions at K49A ***OR*** D71A ***OR*** R74A ***OR*** H77A (see, instant specification at, for example page 73, Table 4).

Indeed, given the disclosure of the instant specification that each of the 1D3, 1F3 and 3B7 antibodies bind a different IFNAR2 epitope, and further given that some of the IFNAR2 substitutions recited in the instant claims actually ***increased*** the binding of each of 1D3, 1F3 and 3B7 and ***polyclonal anti-IFNAR2 antibodies in some instances, see for example, H77A***, the skilled artisan would be highly uncertain about how to proceed to make anti-IFNAR2 antibodies having the limitations of claim 24 which do not bind IFNAR2 K153A **OR** having the limitations of claims 25 and 26 which do not bind to IFNAR2 K49A ***OR*** D71A ***OR*** R74A ***OR*** H77A without undue experimentation (see, instant specification at, for example page 73, Table 4).

The difficulty of isolating antibodies that do not bind ***single*** alanine substitution mutants of IFNAR2 is confirmed by the post filing date publication of Chuntharapai et al. (J Immunol. 1999 Jul 15;163(2):766-73) which states, "[h]owever, in the more detailed analysis of single alanine substitution mutants, we were not able to detect any single residue that had a significant effect on the binding of these mAbs [referring to, among others, the 1D3, 1F3 and 3B7 antibodies]. This suggests that ***multiple regions*** of hIFNAR2-IgG are involved in mAb binding and that the regions on hIFNAR2 interacting with mAbs are much larger than the region interacting with hIFN-a2/a1 as shown in other systems." (See, in particular, page 770, left column).

The instant specification does not provide guidance or direction which particular IFNAR2 domain or peptide should be used to make antibodies with the desired properties. As taught by Janeway et al., either an intact polypeptide or polypeptide domain or a linear peptide can be used to raise antibodies, and the resultant antibodies can recognize antigens via both linear

and conformational epitopes. (see Janeway et al., Immunobiology, 3rd Ed., Garland Science, pp. 3:9-3:11 (1997).

Thus, the instant specification does not provide sufficient guidance or direction beyond demonstrating that immunization with a fusion protein consisting of the extracellular domain of IFNAR2 fused to Fc would ***not*** be a good starting point to make some of the antibodies encompassed by the instant claims.

Thus, undue experimentation would be required to produce the claimed invention commensurate with the scope of the claims from the written disclosure alone. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 24-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a New Grounds of Rejection necessitated by applicant's amendment to the claims.

Claims 24-26, recite an anti-IFNAR2 antibody which "***does not bind to IFNAR2*** comprising an alanine substitution at one or more amino acids..."

Claims to an anti-IFNAR2 antibody that "***does not bind to IFNAR2",*** given their broadest reasonable interpretation consistent with the instant specification, read on anti-IFNAR2 antibody that ***binds an IFNAR2 alanine mutant with less than at or about 90% of the activity with which it binds wild type hIFNAR2***. See instant specification at page 29, 1st paragraph.

However, the disclosure of the instant specification is insufficient to demonstrate possession of the entire genus of claimed antibodies.

In particular, while the instant specification discloses, for example, an antibody that blocks the binding of a first type I interferon to IFNAR2, but does not block the binding of a second type I interferon to IFNAR2, such as IFNβ, and which exhibits binding activity with IFNAR2 comprising an alanine at amino acids 133, 134, 135 and 139 which is less than at or about 10% of the binding that this particular antibody would have for wt IFNAR2 (see instant specification at page 72, table 3, row 7, and the 1D3 antibody), the instant specification does disclose how to make ***all*** of the antibodies encompassed by the instant claims that ***bind an IFNAR2 containing one or more alanine substitutions with less than at or about 90% of the activity with which the antibody binds wild type hIFNAR2.***

For example, the only antibody disclosed in the instant specification that may meet the limitations of claim 24 regarding anti-viral activity, the 1D3 antibody ***binds*** to IFNAR2 with a substitution at K153A (see, instant specification, for example page 73, Table 4).

Moreover, the antibodies exemplified in the instant specification that meet the antiviral limitation of claims 25 and 26, such as the 1D3, 1F3 and 3B7 monoclonal antibodies as well as the disclosed polyclonal anti-IFNAR2 antisera, all ***bind*** to IFNAR2 with substitutions at K49A ***OR*** D71A ***OR*** R74A ***OR*** H77A (see, instant specification at, for example page 73, Table 4).

Thus, the instant claims encompass in their breadth a potentially unbounded genus of anti-IFNAR2 antibodies that do not bind IFNAR2 with a mutation at K153A and having the other limitations of claim 24 **OR** antibodies that do not bind IFNAR2 with mutations at K49A OR D71A OR R74A OR H77A and having the other limitations of claims 25 and 26.

However, given the disclosure of the instant specification that each of the 1D3, 1F3 and 3B7 antibodies bind a different IFNAR2 epitope, and further given that some of the IFNAR2 substitutions recited in the instant claims actually ***increased*** the binding of each of 1D3, 1F3 and 3B7 and ***polyclonal anti-IFNAR2 antibodies in some instances, see for example, H77A***, the skilled artisan would be concerned that it is not possible to create anti-IFNAR2 antibodies that ***bind certain IFNAR2 alanine mutants with less than at or about 90% of the activity with which these antibodies would bind wild type hIFNAR2.***

The instant specification does not provide guidance or direction which particular IFNAR2 domain or peptide should be used to make antibodies with the desired properties. As taught by Janeway et al., either an intact polypeptide or polypeptide domain or a linear peptide can be used to raise antibodies, and the resultant antibodies can recognize antigens via both linear and conformational epitopes. (see Janeway et al., Immunobiology, 3rd Ed., Garland Science, pp. 3:9-3:11 (1997).

Thus, the instant specification does not provide sufficient guidance or direction beyond demonstrating that immunization with a fusion protein consisting of the extracellular domain of IFNAR2 fused to Fc would ***not*** be a good starting point to gain possession of antibodies encompassed by the breadth of the instant claims.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, MPEP 2163 II.A.3a.ii.

See also, Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997), "Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. Claim 3 stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, essentially for the reasons of record.

Applicant's arguments have been considered in their entirety, but have not been found convincing, essentially for the reasons of record.

In particular, Applicant argues that the instant specification describes polypeptides comprising antigen binding fragments, such as fusion proteins to viral coat protein used in phage display and antigen binding fragments labeled with biotin and alkaline phosphatase. Applicant further asserts that bispecific molecules such as a Fab and an immunoadhesin as well as peptide tagged antibodies are known in the art.

Applicant's argument has been considered but has not been found convincing, essentially for the reasons of record.

The disclosure of a limited number of species of the claimed invention, e.g., fusions of antigen binding fragments to viral coat protein or antibodies labeled with biotin, alkaline phosphatase, or a peptide tag is not sufficient to demonstrate possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the limited number of species disclosed and the extensive variation permitted within the genus of polypeptides.

The claim recites the genus of polypeptides "comprising a portion of the antibody of claim 1" but does not recite a physical structure or testable functional activity for the polypeptides.

The claimed polypeptides "comprising a portion of the antibody of claim 1" lack a common structure essential for their function and the claims do not require any particular structure basis or testable functions be shared by the instant polypeptides "comprising a portion of the antibody of claim 1".

Thus, the genus of polypeptides "comprising a portion of the antibody of claim 1" is extremely large, far larger than antibodies fused to viral coat proteins and labeled antibodies.

"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997).

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406.

In the absence of disclosure of relevant, identifying characteristics of the polypeptides "comprising a portion of the antibody of claim 1 or 2" there is insufficient written disclosure under 35 U.S.C. 112, first paragraph.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 1115).

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b).the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. **Claims 1, 5-8 and 15, 17, 19, 21 and 23 stand rejected, and claims 9, 14 and 24-29 are rejected under 35 U.S.C. 102(b)** as anticipated by Chuntharapai et al. (FASEB Journal, abstract #1877, 10(6):A1325, April 30, 1996) as evidenced by the instant specification at pages 69-76 and Chuntharapai et al. (J Immunol. 1999 Jul 15;163(2):766-73)(see entire documents).

This is a New Grounds of Rejection necessitated by applicant's amendment to the instant claims.

Applicant's arguments have been considered but have not been found convincing, essentially for the reasons of record.

In particular, applicant argues that Chuntharapai does not disclose the characteristics of the 1D3, 1F3 and 3B7 antibodies as claimed.

Applicant's argument has been considered but has not been found convincing, essentially for the reasons of record.

As essentially stated in the Office Action of August 18, 2006, Chuntharapai teaches the creation of anti-IFNAR2 monoclonal antibodies 1D3, 1F3 and 3B7 by immunizing mice with IFNAR2-IgG (referred to as "the IFNARII-IgG" by Chuntharapai), and teaches that monoclonal antibody 1D3 does not block IFNα-1/2 binding or the anti-viral activity of various interferons, while the 1F3 and 3B7 antibodies block these activities.

Chuntharapai does not have to explicitly disclose the properties of the instantly claimed antibodies in order to anticipate the instant claims because, as stated in the M.P.E.P. § 2112.01, "products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)." Thus, The 1D3, 1F3 and 3B7 monoclonal antibodies described by Chuntharapai *inherently* have the biological activities recited in the instant claims as evidenced by the instant specification at pages 69-71 as well as Chuntharapai et al. (1999).

Moreover, applicant asserts that they believe that the hybridomas producing monoclonal antibodies 1D3, 1F3 and 3B7 were not made publicly available prior to October 6, 1997, the filing date of USSN 60/061,185.

Applicant's statement concerning the public availability of the hybridomas producing the 1D3, 1F3 and 3B7 monoclonal antibodies has been considered but has not been found convincing, essentially for the reasons of record.

Applicant's statement is not found convincing because it is not clear if it is being made by a person in position to corroborate the public availability of the 1D3, 1F3 or 3B7 antibodies produced by the claimed hybridomas, or the public availability of the hybridomas themselves. In particular, the statement can not be made by just any inventor(s), or possibly even by the assignee(s), rather it must be made by an inventor(s) or an assignee(s) ***in a position to corroborate the fact*** that these biological materials were not made publicly available, in the absence of a signed confidentiality agreement, before October 6, 1997 (the effective filing date of the instant application).

Thus, in the absence of objective evidence or assurances by one in a position to collaborate the fact that the 1D3, 1F3 or 3B7 antibodies produced by the claimed hybridomas, or the hybridomas themselves hybridomas were not made available to the participants of the conference which was the basis for the Chuntharapai abstract publication of October 6, 1997, or the general public, e.g., in the absence of a signed confidentiality agreement, before October 6, 1997, the effective filing date of the instant application, it is assumed for the purposes of this rejection that the Chuntharapai abstract publication enabled one of skill in the art to also make the 1D3, 1F3 and 3B7 anti-IFNAR2 antibodies made by the particular hybridoma cell lines recited in claim 1.

With respect to claims 24-26 it is noted that while Chuntharapai does not recite that the 1D3, 1F3 and 3B7 antibodies do not bind to IFNAR2 with alanine substitutions at particular positions, these antibodies inherently fail to bind IFNAR2 with alanine substitutions at particular positions as evidenced by the instant specification, in particular page 72, Table 3.

It is further noted that with respect to claim 14, Chuntharapai teaches that the 1D3, 1F3 and 3B7 Mabs were used in flow cytometry, ELISA and antiviral assays, thus composition of the Mabs and an excipient, such as water, were prepared (note that the only criteria for an excipient put forth in the instant specification is that it be nontoxic to recipients, see page 58, 2nd paragraph).

Lastly, with respect to claims 27-29, the antibodies of Chuntharapai comprise the CDRs of the antibody 1F3, 1D3 and 3B7 and thus they anticipate these claims as well.

Thus, Chuntharapai (1996) anticipates the instant claims.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. **Claims 1, 3, 5-8, 15, 17, 19, 21 and 23 stand rejected, and claims 9, 14 and 24-29 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Chuntharapai et al. (FASEB Journal, abstract #1877, 10(6):A1325, April 30, 1996), in view of Novick et al. (U.S. Patent No. 6,458,932), the instant specification at pages 69-76 and Chuntharapai et al. (J Immunol. 1999 Jul 15;163(2):766-73)(see entire documents).

This is a New Grounds of Rejection necessitated by applicant's amendment to the instant claims.

Applicant's arguments have been considered but have not been found convincing, essentially for the reasons of record.

In particular, applicant argues that the Chuntharapai abstract does not disclose the characteristics of the 1D3, 1F3 and 3B7 antibodies as claimed, and that Chuntharapai fails to disclose the public availability of the antibodies or the hybridomas that produce the antibodies. Applicant further argues that Novick does not remedy the deficiencies of Chuntharapai, in particular that Novick does not teach making an antibody that does not bind a first Type I interferon.

Applicant's argument has been considered but has not been found convincing, essentially for the reasons of record.

As stated above, the 1D3, 1F3 and 3B7 monoclonal antibodies described by Chuntharapai have the biological activities recited in the instant claims in view of the instant specification at pages 69-76 and well as Chuntharapai et al. Therefore, the antibodies taught by Chuntharapai must have the properties recited in the instant claims.

Moreover, as stated above, given no assurances by one in position to collaborate the fact that the 1D3, 1F3 or 3B7 antibodies produced by the claimed hybridomas, or the hybridomas themselves hybridomas were not made available to the participants of the conference which was the basis for the Chuntharapai abstract publication of October 6, 1997, or the general public (in the absence of a signed confidentiality agreement), before October 6, 1997, the effective filing date of the instant application, it is assumed for the purposes of this rejection that the Chuntharapai abstract publication enabled one of skill in the art to also make the 1D3, 1F3 and 3B7 anti-IFNAR2 antibodies made by the particular hybridoma cell lines recited in claim 1.

Furthermore, with respect to claims 9, 14 and 24-29, it is noted that the teachings of Chuntharapai and the instant specification are given above.

Accordingly, the instant claims are unpatentable over Chuntharapai in view of Novick and the instant specification.

16. **Claims 25 is rejected under 35 U.S.C. 102(b)** as anticipated by Colamonici et al. (J Biol Chem. 1993 May 25;268(15):10895-9)(see entire document), as evidenced by Bekisz et al. (Growth Factors. 2004 Dec;22(4):243-51), Chuntharapai et al. (J Immunol. 1999 Jul 15;163(2):766-73) and the instant specification at pages 2 and 69-76 (see entire document).

This is a New Grounds of Rejection necessitated by applicant's amendment to the claims.

Colamonici teaches an anti-IFNAR2 antibody, referred to as the "IFNaRβ1" monoclonal antibody ("IFNaRβ1" is the same as "IFNAR2" as evidenced by the instant specification at page 2, 4th paragraph), that blocks the ability of IFNα2 to bind IFNAR2.

Given that the anti-IFNAR2 antibody of Colamonici blocks the binding activity of IFNα2 for IFNAR2, and further given that the antiproliferative, antiviral and immunomodulatory activities induced by the interferons are all dependent upon IFNAR2 binding as evidenced by Bekisz (see, Bekisz, in particular page 244, Figure 1), the anti-IFNAR2 antibody of Colamonici will *inherently* block the antiviral activity of a first type I interferon.

Moreover, given that an alanine at one or more positions 49, 51, 52, 54, 68, 71 and 72 of IFNAR2, in particular at D68A, disrupts the binding of IFN-α2/1, the 1D3, 1F3 and 3B7 monoclonal antibodies and polyclonal anti-IFNAR2 antisera as evidenced by the instant specification at page 73 and as further evidenced by Chuntharapai which teaches that "D68 may be ***structurally important***, as mutations of it affect the binding of ligand and all three mAbs," see Chuntharapai, in particular page 769, right column, 1st paragraph and page 770 Table 5, the antibody of Colamonici would *inherently* **not** bind IFNAR2 comprising an alanine at one or more positions 49, 51, 52, 54, 68, 71 and 72 since IFNAR2 containing an alanine at position 68 is by all measures structurally different.

Thus, the anti-IFNAR2 antibody of Colamonici anticipates the instantly claimed anti-IFNAR2 antibodies.

Since the Office does not have a laboratory to test the reference antibody, it is applicant's burden to show that the reference antibody ***does not block*** the antiviral activity of a Type I interferon and ***does bind*** to IFNAR2 comprising an alanine at one or more positions 49, 51, 52, 54, 68, 71 and 72. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

17. No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
March 28, 2007

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TC 1600
3/30/07